

WHAT IS CLAIMED IS:

1. A method for inhibiting bacterial growth, comprising contacting a bacterium with an antibacterial compound that specifically binds to a bacteriophage polypeptide binding domain
5 of *Staphylococcus aureus* primary sigma factor polypeptide, wherein said bacteriophage polypeptide binding domain comprises an amino acid sequence selected from the group consisting of:
 - (i) the amino acid sequence set forth in SEQ ID NO: 3;
 - (ii) the amino acid sequence set forth in SEQ ID NO: 4;
 - 10 (iii) the amino acid sequence set forth in SEQ ID NO: 5;
 - (iv) a fragment of (i) or (ii) containing said bacteriophage polypeptide binding domain; and
 - (v) a variant having at least 95% sequence identity with one of (i), (ii), (iii), and (iv), and containing a domain that is bound by said bacteriophage polypeptide.
- 15 2. The method according to claim 1, wherein said compound is a polypeptide selected from the group consisting of the polypeptide set forth in SEQ ID NO: 7, the polypeptide set forth in SEQ ID NO: 8, a fragment of the polypeptide set forth in SEQ ID NO: 7 or SEQ ID NO: 8, and a variant having at least 95% sequence identity with the polypeptide set forth in SEQ ID
20 NO: 7 or SEQ ID NO: 8, wherein said fragment and said variant specifically bind to said bacteriophage polypeptide binding domain of said *Staphylococcus aureus* primary sigma factor polypeptide.
- 25 3. A method for inhibiting growth of *Staphylococcus aureus*, comprising contacting a *Staphylococcus aureus* bacterium with an antibacterial compound that specifically binds to a bacteriophage polypeptide binding domain of *Staphylococcus aureus* primary sigma factor polypeptide, wherein said bacteriophage polypeptide binding domain comprises an amino acid sequence selected from the group consisting of:
 - (i) the amino acid sequence set forth in SEQ ID NO: 3;
 - 30 (ii) the amino acid sequence set forth in SEQ ID NO: 4; and
 - (iii) the amino acid sequence set forth in SEQ ID NO: 5.
4. An isolated or purified fragment of the *S. aureus* primary sigma factor polypeptide set forth in SEQ ID NO: 2, wherein said fragment comprises a bacteriophage polypeptide binding
35 domain.

5. The fragment of claim 4, wherein said bacteriophage polypeptide binding domain comprises from about 67 to about 245 amino acids.
- 5 6. The fragment claim 4 , wherein said a bacteriophage polypeptide binding domain is bound by the bacteriophage polypeptide set forth in SEQ ID NO:7 and/or the bacteriophage polypeptide set forth in SEQ ID NO:8.
7. The fragment of claim 4, wherein said bacteriophage polypeptide binding domain
10 comprises an amino acid sequence selected from the group consisting of:
- (i) the amino acid sequence set forth in SEQ ID NO: 3;
 - (ii) the amino acid sequence set forth in SEQ ID NO: 4; and
 - (iii) the amino acid sequence set forth in SEQ ID NO: 5.
- 15 8. An isolated or purified fragment of the *S. aureus* primary sigma factor polypeptide set forth in SEQ ID NO: 2, wherein said fragment comprises a bacteriophage polypeptide binding domain comprising an amino acid sequence selected from the group consisting of:
- (i) the amino acid sequence set forth in SEQ ID NO: 3;
 - (ii) the amino acid sequence set forth in SEQ ID NO: 4;

20 (iii) the amino acid sequence set forth in SEQ ID NO: 5;

 - (iv) a fragment having at least 50 contiguous amino acids of (i) or (ii), and containing said bacteriophage polypeptide binding domain; and
 - (v) a variant having at least 95% sequence identity with one of (i), (ii), (iii), and (iv), and containing a domain that is bound by said bacteriophage polypeptide.
- 25 9. An isolated or purified bacteriophage polypeptide that binds the *Staphylococcus aureus* primary sigma factor polypeptide set forth in SEQ ID NO: 2.
10. An isolated or purified polypeptide comprising at least 10 contiguous amino acids of the
30 amino acid sequence set forth in SEQ ID NO: 7, wherein said polypeptide binds the *Staphylococcus aureus* primary sigma factor polypeptide set forth in SEQ ID NO: 2, and/or wherein said polypeptide inhibits growth of *S. aureus*.
11. An isolated or purified polypeptide comprising an amino acid sequence having at least
35 50% sequence identity with the amino acid sequence set forth in SEQ ID NO: 7 or SEQ ID NO:

8, wherein said polypeptide binds the *Staphylococcus aureus* primary sigma factor polypeptide set forth in SEQ ID NO: 2, and/or wherein said polypeptide inhibits growth of *S. aureus*.

12. The polypeptide of claim 11, wherein said sequence identity is at least 75%.

13. The polypeptide of claim 11, wherein said sequence identity is at least 95%.

14. An isolated or purified polypeptide comprising amino acids 1-198 of SEQ ID NO: 7 or amino acids 1-149 of SEQ ID NO: 8.

15. A screening method comprising:

(a) contacting a *Staphylococcus aureus* primary sigma factor polypeptide comprising a bacteriophage binding domain with a test compound in the presence of a bacteriophage polypeptide that specifically binds to said bacteriophage binding domain; and

(b) determining whether the test compound inhibits binding of said bacteriophage polypeptide to said bacteriophage binding domain.

16. The screening method of claim 15, wherein said bacteriophage binding domain comprises an amino acid sequence selected from the group consisting of:

(i) the amino acid sequence set forth in SEQ ID NO: 3;

(ii) the amino acid sequence set forth in SEQ ID NO: 4;

(iii) the amino acid sequence set forth in SEQ ID NO: 5;

(iv) a fragment of (i) or (ii) containing said bacteriophage polypeptide binding domain; and

(v) a variant having at least 95% sequence identity with one of (i), (ii), (iii), and (iv) and containing a domain that is bound by said bacteriophage polypeptide.

17. The screening method of claim 15, wherein said bacteriophage polypeptide is a polypeptide of bacteriophage G1.

18. The screening method of claim 17, wherein said bacteriophage polypeptide comprises amino acids 1-198 of SEQ ID NO: 7 or amino acids 1-149 of SEQ ID NO: 8.

19. The screening method of claim 15, further comprising measuring ability of the test compound to inhibit DNA binding by said *Staphylococcus aureus* primary sigma factor polypeptide.
- 5 20. The screening method of claim 15, further comprising measuring ability of the test compound to inhibit binding between: (i) said *Staphylococcus aureus* primary sigma factor polypeptide; and (ii) *S. aureus* Core-RNA polymerase.
21. The screening method of claims 15, further comprising measuring ability of the test
10 compound to inhibit *S. aureus* RNA polymerase activity.
22. The screening method of claim 15, further comprising measuring bactericidal or bacteriostatic activity of the test compound.
- 15 23. The screening method of claim 15, wherein said determining is carried out using a technique selected from the group consisting of Fluorescence Resonance Energy Transfer (FRET), fluorescence polarization, surface plasmon resonance, scintillation proximity assay, biosensor assay, isothermal titration microcalorimetry and phage display.
- 20 24. The screening method of claim 15, wherein said test compound is selected from the group consisting of a small molecule, a peptidomimetic compound, a peptide and a polypeptide.
25. A screening method comprising:
- 25 (a) contacting (i) a first polypeptide binding domain, (ii) a second polypeptide binding domain and (iii) at least one test compound, wherein said first and second polypeptide binding domains bind specifically with each other,
wherein said first polypeptide binding domain comprises an amino acid sequence selected from the group consisting of: the amino acid sequence set forth in
30 SEQ ID NO: 3; the amino acid sequence set forth in SEQ ID NO: 4; and the amino acid sequence set forth in SEQ ID NO: 5;
wherein said second polypeptide binding domain comprises the amino acid sequence set forth in SEQ ID NO: 7 or SEQ ID NO: 8; and
- (b) determining whether said at least one test compound inhibits binding
35 between said first and second polypeptide binding domains.

26. An isolated or purified polynucleotide comprising at least 25 contiguous nucleotides of the nucleic acid sequence set forth in SEQ ID NO: 6, wherein said polynucleotide encodes a polypeptide that binds the *Staphylococcus aureus* primary sigma factor polypeptide set forth in SEQ. ID NO: 2, and/or wherein said polynucleotide encodes a polypeptide that inhibits growth of *S. aureus*.
27. An isolated or purified nucleic acid molecule having at least 50% sequence identity with the nucleic acid sequence set forth in SEQ ID NO: 6, wherein said nucleic acid molecule encodes a polypeptide that binds the *Staphylococcus aureus* primary sigma factor polypeptide set forth in SEQ. ID NO: 2, and/or wherein said nucleic acid molecule encodes a polypeptide that inhibits growth of *S. aureus*.
28. The nucleic acid molecule of claim 27, wherein said sequence identity is at least 75%.
29. The nucleic acid molecule of claim 27, wherein said sequence identity is at least 95%.
30. An isolated or purified polynucleotide comprising nucleotides 1-597 of SEQ ID NO: 6.
31. An antibacterial compound which inhibits *S. aureus* primary sigma factor-dependent RNA polymerase activity, wherein said compound binds a bacteriophage binding domain of *S. aureus* primary sigma factor, and wherein said bacteriophage binding domain comprises an amino acid sequence selected from the group consisting of: the amino acid sequence set forth in SEQ ID NO: 3; the amino acid sequence set forth in SEQ ID NO: 4; and the amino acid sequence set forth in SEQ ID NO: 5.
32. An antibacterial compound which inhibits DNA binding activity of a *S. aureus* primary sigma factor, wherein said compound binds a bacteriophage binding domain of *S. aureus* primary sigma factor, and wherein said bacteriophage binding domain comprises an amino acid sequence selected from the group consisting of: the amino acid sequence set forth in SEQ ID NO: 3; the amino acid sequence set forth in SEQ ID NO: 4; and the amino acid sequence set forth in SEQ ID NO: 5.

33. The antibacterial compound of claim 32, wherein said compound mimics the inhibitory activity, and/or the bactericidal or bacteriostatic effect, of the bacteriophage polypeptide comprising amino acids 1-198 of SEQ ID NO: 7 or amino acids 50-198 of SEQ ID NO: 8.

5 34. An antibacterial compound that has a bactericidal or bacteriostatic effect on *Staphylococcus aureus* bacteria, wherein said compound binds a bacteriophage binding domain of *S. aureus* primary sigma factor, and wherein said bacteriophage binding domain comprises an amino acid sequence selected from the group consisting of: the amino acid
10 sequence set forth in SEQ ID NO: 3; the amino acid sequence set forth in SEQ ID NO: 4; and the amino acid sequence set forth in SEQ ID NO: 5.

35. The antibacterial compound of claim 34, wherein said compound mimics the inhibitory activity, and/or the bactericidal or bacteriostatic effect, of the bacteriophage polypeptide comprising amino acids 1-198 of SEQ ID NO: 7 or amino acids 50-198 of SEQ ID NO: 8.
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